Appl. No.
Filed

: 09/292,437 : April 15, 1999

Remarks

Before the present amendment, claims 1-97 were pending in this application. Claims 1-7 and 26-97 were withdrawn from consideration as being drawn to a non-elected invention, and claims 1-25 were under examination. The current amendment includes the cancellation of claims 11-13, 17, 21, and 25, and the amendment of claims 8, 9 and 10. The amendments do not add new matter.

## The Office Action

#### 1. Election/Restriction

Applicants note the finality of the election of the invention of Group II, claims 8-25, and nucleotide sequences encoding the protein of SEQ ID NO: 3. Applicants maintain that the requirement to limit the nucleotide sequences examined in the present as indicated in improper in view of applicants' earlier arguments and also in view of the Commissioner's decision to permit the examination of a reasonable number of nucleotide sequences in a single application (See Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 (November 19, 1996), and M.P.E.P. 803.04). Applicants specifically reserve the right to petition to the Commissioner to review the requirement, but elect to defer the filing of such petition until after final action on or allowance of claims to the invention elected, as provided in 37 C.F.R. 1.144.

#### 2. Claim Rejections – 35 U.S.C. § 101

Claims 8-13 were rejected as being directed to non-statutory subject matter, since they were directed to the nucleic acid sequence, which "has the same characteristic and utility as the nucleic acid sequence found naturally." The cancellation of claims 11-13 and the amendment of claims 8-10 to recite an "isolated nucleic acid molecule" is believed to overcome this rejection.

## 3. Claim Rejections – 35 U.S.C. § 112

(1) Claims 11-13, 17, 21, and 25 were rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of adequate written description for the invention to which these claims were directed. The cancellation of these claims moots their rejection. It is emphasized, however, that these claims were canceled merely to facilitate the prosecution of the present application, and without acquiescence in their rejection, or in any aspects of the Examiner's position. Applicants

Appi. No. Filed

: 09/292,4

: April 15, 1999

specifically reserve the right to pursue the subject matter of the claims canceled in one or more continuing applications.

- (2) Claims 10-13, 16-17, 20-21, and 24-25 were rejected under 35 U.S.C. § 112, second paragraph as "indefinite" in the recitation of "substantially hydrophobic domain." Without acquiescing in the Examiner's position, claims 11-13, 17, 21, and 25 have been canceled, which moots their rejection. As the remaining claims no longer recite the phrase objected to, the Examiner is respectfully requested to withdraw their rejection.
- (3) Claims 10-13, 16-17, and 24-25 were rejected under 35 U.S.C. § 112, second paragraph as "indefinite" in their recitation of the phrases "at least 31 amino acids carboxyl to the motif" and "residues 31-33 from the motif." Claims 11-13, 17, 21, and 25 have been canceled, and remaining claims have been amended so that they no longer recite the phrases objected to. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.
- (4) Claims 11-13, 17-21, and 25 were rejected under 35 U.S.C. § 112, second paragraph as being "indefinite" in their recitation of the phrase "stringent conditions." Without acquiescence in the Examiner's position, claims 11-13, 17, 21, and 25 have been canceled, which moots their rejection.
- (5) Claims 8-25 were rejected under 35 U.S.C. § 112, second paragraph in their recitations of "substantially purified" sortase transamidase. The cancellation of claims 11-13, 17-21, and 25, and the current amendment of the remaining claims is believed to overcome this rejection, the withdrawal of which is respectfully requested.
- (6) Claims 11-13 were rejected under 35 U.S.C. § 112, second paragraph for their recitation of the phrase "greater than about." The cancellation of claims 11-13, which was done without prejudice, moots their rejection.

#### 4. Claim Rejections – 35 U.S.C. § 102

Claims 11-13, 17, 21, and 25 were rejected under 35 U.S.C. § 102(b) as "being anticipated by Kunsch et al." (EP 786529). The cancellation of claims 11-13, 17, 21, and 25 moots this rejection. It is emphasized, however, that this cancellation should by no means be interpreted as acquiescence in the present rejection, or the rejection of the canceled claims under any other ground.

Appi. No.

09/292,437

· Filed

April 15, 1999

## 5. <u>Double Patenting</u>

According to the Examiner, claims 9, 15, 19, and 23 are "substantially duplicate" of claims 8, 14, 18, and 22. Applicants respectfully disagree, and traverse this rejection.

The Examiner will appreciate that claims 8 and 9 do not cover "the same thing," and differ in much more than in a slight difference of wording. Indeed, the literal scope of claim 8 covers isolated nucleic acid molecules encoding a polypeptide comprising SEQ ID NO: 3, and certain variants of such polypeptide, comprising well-defined conservative amino acid substitutions. Claim 9, which is dependent on claim 8, is directed to isolated nucleic acid molecules encoding a polypeptide comprising SEQ ID NO: 3. Accordingly, the Examiner is respectfully requested the reconsider and withdraw the present rejection.

Applicants believe that all claims pending in this application are in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Appended to the present amendment are sheets entitled "Version with Markings to Show Changes Made."

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: By:

Ginger R. Dreger Registration No. 33,055 Attorney of Record 620 Newport Center Drive Sixteenth Floor Newport Beach, CA 92660

(415) 954-4114

Appl. No.

09/292,437

Filed : April 15, 1999

# Version with Markings to Show Changes Made

Claims 11-13, 17, 21, and 25 have been canceled.

Claims 8, 9, and 10 have been amended as follows:

- 8. (Amended) [A] <u>An isolated</u> nucleic acid [sequence] <u>molecule</u> encoding a <u>sortase-transamidase</u> [the] enzyme [of claim 6] <u>from a Gram-positive bacterium</u>, wherein the enzyme comprises an amino acid sequence selected from the group consisting of: (1) M-K-K-W-T-N-R-L-M-T-I-A-G-V-V-L-I-L-V-A-A-Y-L-F-A-K-P-H-I-D-N-Y-L-H-D-K-D-K-D-E-K-I-E-Q-Y-D-K-N-V-K-E-Q-A-S-K-D-K-K-Q-Q-A-K-P-Q-I-P-K-D-K-S-K-V-A-G-Y-I-E-I-P-D-A-D-I-K-E-P-V-Y-G-P-A-T-P-E-Q-L-N-R-G-V-S-F-A-E-E-N-E-S-L-D-D-Q-N-I-S-I-A-G-H-T-F-I-D-R-P-N-Y-Q-F-T-N-L-K-A-A-K-K-G-S-M-V-Y-F-K-V-G-N-E-T-R-K-Y-K-M-T-S-I-R-D-V-K-P-T-D-V-G-V-L-D-E-Q-K-G-K-D-K-Q-L-T-L-I-T-C-D-D-Y-N-E-K-T-G-V-W-E-K-R-K-I-F-V-A-T-E-V-K (SEQ ID NO: 3); and (2) sequences incorporating one or more conservative amino acid substitutions in SEQ ID NO: 3, wherein the conservative amino acid substitutions are any of the following: (1) any of isoleucine, leucine, and valine for any other of these amino acids; (2) aspartic acid for glutamic acid and vice versa; (3) glutamine for asparagine and vice versa; and (4) serine for threonine and vice versa.
- 9. (Amended) [A] <u>An isolated nucleic acid [sequence] molecule according to [of] claim [7] 8 wherein the amino acid sequence of said enzyme is: M-K-K-W-T-N-R-L-M-T-I-A-G-V-V-L-I-L-V-A-A-Y-L-F-A-K-P-H-I-D-N-Y-L-H-D-K-D-K-D-E-K-I-E-Q-Y-D-K-N-V-K-E-Q-A-S-K-D-K-K-Q-Q-A-K-P-Q-I-P-K-D-K-S-K-V-A-G-Y-I-E-I-P-D-A-D-I-K-E-P-V-Y-G-P-A-T-P-E-Q-L-N-R-G-V-S-F-A-E-E-N-E-S-L-D-D-Q-N-I-S-I-A-G-H-T-F-I-D-R-P-N-Y-Q-F-T-N-L-K-A-A-K-K-G-S-M-V-Y-F-K-V-G-N-E-T-R-K-Y-K-M-T-S-I-R-D-V-K-P-T-D-V-G-V-L-D-E-Q-K-G-K-D-K-Q-L-T-L-I-T-C-D-D-Y-N-E-K-T-G-V-W-E-K-R-K-I-F-V-A-T-E-V-K (SEQ ID NO: 3).</u>
- 10. (Amended) [A] <u>An isolated nucleic acid [sequence] molecule encoding a</u> [substantially purified] sortase-transamidase enzyme from a Gram-positive bacterium, [the enzyme having a molecular weight of about 23,539 daltons and catalyzing a reaction that

Appi. No.

09/292,437

**Filed** 

April 15, 1999

covalently cross-links the carboxyl terminus of a protein having a sorting signal to the peptidoglycan of a Gram-positive bacterium, the sorting signal having: (1) a motif of LPX<sub>3</sub>X<sub>4</sub>G therein; (2) a substantially hydrophobic domain of at least 31 amino acids carboxyl to the motif; and (3) a charged tail region with at least two positively charged residues carboxyl to the substantially hydrophobic domain, at least one of the two positively charged residues being arginine, the two positively charged residues being located at residues 31-33 from the motif. wherein X<sub>3</sub> is any of the twenty naturally-occurring L-amino acids and X<sub>4</sub> is selected from the group consisting of alanine, serine, and threonine, and wherein sorting occurs by cleavage between the fourth and fifth residues of the LPX<sub>3</sub>X<sub>4</sub>G motif, wherein the nucleic acid sequence includes therein comprising a sequence selected from the group consisting of: (1) ATGAAAAATGGACAAATCGATTAATGACAATCGCTGGTGTGGTACTTATCCTAGTG GCAGCATATTTGTTTGCTAAACCACATATCGATAATTATCTTCACGATAAAGATAAA GATGAAAAGATTGAACAATATGATAAAAATGTAAAAGAACAGGCGAGTAAAGATA AAAAGCAGCAAGCTAAACCTCAAATTCCGAAAGATAAATCGAAAGTGGCAGGCTAT ATTGAAATTCCAGATGCTGATATTAAAGAACCAGTATATCCAGGACCAGCAACACCT GAACAATTAAATAGAGGTGTAAGCTTTGCAGAAGAAAATGAATCACTAGATGATCA AAATATTTCAATTGCAGGACACACTTTCATTGACCGTCCGAACTATCAATTTACAAA TCTTAAAGCAGCCAAAAAAGGTAGTATGGTGTACTTTAAAGTTGGTAATGAAACAC GTAAGTATAAAATGACAAGTATAAGAGATGTTAAGCCTACAGATGTAGGAGTTCTA GATGAACAAAAGGTAAAGATAAACAATTAACATTAATTACTTGTGATGATTACAA TGAAAAGACAGGCGTTTGGGAAAAACGTAAAATCTTTGTAGCTACAGAAGTCAAAT AA (SEQ ID NO: 2); or (2) a sequence complementary to SEQ ID NO: 2.

W:\DOCS\GRD\GRD-7236.DOC 012202